

## Letter to the Editors

## Case discussion of an immediate serious reaction to hexavalent vaccine mistaken for anaphylaxis

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Anaphylaxis is rarely associated with vaccination. Clinical presentation may include a variety of non-specific symptoms, making a clinical diagnosis uncertain. Therefore, it is important to distinguish anaphylaxis from other adverse events following immunization (AEFIs), particularly in children, to manage subsequent immunizations where necessary. For administration of additional doses a specialist evaluation is recommended to confirm the diagnosis and consider if re-vaccination is appropriate. A post-event evaluation is based on an in-depth history and skin and *in vitro* testing to identify specific sensitizations. Applying a standardized AEFI case definition, such as the Brighton Collaboration [1], is also helpful for individual cases as well as pharmacovigilance activities.

We describe the case of a child with an immediate reaction to hexavalent vaccine which was mistakenly diagnosed as anaphylaxis. The baby, born in the 34th week, reported no perinatal problems and was breast and artificial milk fed. In good health, he received the first dose of hexavalent vaccine (diphtheria-tetanus-pertussis-polio-hepatitis B-haemophilus influenzae type B) at 3 months of age. Upon injection he cried, then he manifested atony, pallor, apnoea and flaccidity. Treated with mouth-to-mouth ventilation, he responded by crying, gasping, ocular reversion and generalized hypotonia. He was then treated with intramuscular epinephrine. On arrival in the emergency department, oxygen was administered and he became responsive, reactive and began to breathe normally. He was treated with i.m. methylprednisolone. A transient papular skin rash was observed on the trunk. The vaccination schedule was interrupted and he was referred to a specialized consultation service [2] for further vaccination. Serum analysis showed total IgE = 10 kU l<sup>-1</sup> and IgE level to tetanus toxoid <0.10 kUA l<sup>-1</sup> (Unicap, Phadia, Sweden). Since there were doubts about the anaphylaxis diagnosis,

the following hypotheses were evaluated with international vaccine safety collaborators:

- Anaphylaxis*: the diagnosis was unlikely because the symptoms and signs did not fulfil the Brighton anaphylaxis case definition. Skin changes were not typical of a hypersensitivity reaction nor did he manifest respiratory or cardiovascular features. Additional factors which make this unlikely include his initial response to mouth-to-mouth ventilation prior to administration of epinephrine and this was his first exposure to the hexavalent vaccine.
- Hypotonic-hyporesponsive episode (HHE)*: he had pallor, hyporesponsiveness and hypotonia, which are symptoms of HHE, but also apnoea, which is not part of HHE [3].
- Apparent life-threatening event (ALTE)*: sudden episode of a combination of apnoea, change in colour, change in muscle tone, coughing or gagging [4].
- Apnoea in ex-premature infant*: condition described in infants mostly born before and up to 32 weeks gestation; immunization is one of the triggers [5].
- Reflex Anoxic Seizure*: exaggerated vagal response to pain resulting in extreme bradycardia or even asystole, possibly causing post-vaccination collapse [6].

This was considered the most likely hypothesis, but skin testing was performed with hexavalent vaccine and was negative. As a precaution hexavalent vaccine was consequently administered in two graded doses (0.1 and 0.4 ml), without subsequent reactions.

Anaphylaxis is often considered to be the cause of acute and unexpected events following immunization in infants. Careful consideration of the history, application of Brighton Collaboration case definition and specialist evaluation allows for accurate diagnosis [7]. If anaphylaxis is excluded, revaccination under supervision should be

All authors significantly contributed in the management of this case and therefore their names should be included.

considered. This case illustrates these issues because anaphylaxis was excluded. Data on outcome of revaccinations in particular situations and on AEFI surveillance activities should be shared at a global level.

## Competing interests

There are no competing interests to declare.

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